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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,400	07/22/2002	Thomas Hantke	0480/01219	2952

26474 7590 03/01/2006

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EXAMINER

WANG, SHENGJUN

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 03/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/088,400	<b>Applicant(s)</b> HANTKE ET AL.	
	<b>Examiner</b> Shengjun Wang	<b>Art Unit</b> 1617	

**– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –**  
**Period for Reply**

**A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.**

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 13 December 2005.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2,4,6-8,10-16 and 20-25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,4,6-8,10-16 and 20-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 13, 2005 has been entered.

#### ***Claim Rejections 35 U.S.C. 103***

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. Claims 1, 2, 4, 6-8, 10-16, 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andries et al. (US 6,197,779), in view of Goertz et al. (US 4,801,460), Nakamichi et al. (US 5,456,923), Sasatani et al. (US 5,876,760) and Takada (US 5,350,741), and in further view of Baert (EP 0 872 233, IDS)

4. Andries et al. teaches the HIV inhibiting pyrimidine derivatives herein and the method of using the same for preparing pharmaceutical composition, and for treating HIV infection. See, the abstract, cols 1-10, 17-19. The elected compound herein is a preferred compound disclosed by Andries et al. see, col. 10, lines 14-15. The compounds may be formulated into various conventional dosage forms, such as powders, tablet, capsule with solid carrier and other pharmaceutical excipients. See, particularly, col. 18, line 19 to col. 19, line 25. (Applicants also

Art Unit: 1617

admitted the compounds are known in the art, citing PCT/EP99/02043, which is equivalent to US 6,197,779, and PCT EP/02044, see page 2 herein)

5. Andries et al. do not teach expressly the particular dosage form herein with PVP or it's copolymer as carrier and polyoxyethylene hydrogenated castor oil and citric acid as additional excipients, or the particular release forms.

6. However, Goertz et al. teach a solid pharmaceutical form wherein polyvinylpyrrolidone or copolymer of vinylpyrrolidone and vinyl acetate or used as carrier, and a solid solution of the active ingredient is formed. See particularly, the abstract, col. 3, lines 3-31, col. 4, lines 11-45, and the claims. There is no particular limitation as to the active ingredients employed therein. The concentration of active ingredients may be in the range from 0.1 to 95%, with preferred range of 30-70%. 45 to 50% of polymer is used in the particular examples. Other known pharmaceutical excipients may be added accordingly. The forms may be made by extrusion. See, cols. 3-8. Nakamichi et al. teach that solid dispersion or solution is known to be useful for controlling the rate of release of a drug from dosage form or improving the bioavailability of drugs. Nakamichi et al. further teaches that other polymeric material, such as modified cellulose (e.g. hydroxypropylmethylcellulose) are similarly useful (like PVP) as solid carrier, and extrusion is a conventional method for making a solid dispersion or solution form. See, particularly, cols. 1-2, and the claims. Both Sasatani et al. and Takada teaches that polyethylene glycol castor oil ester and citric acid are known pharmaceutical excipients and are particularly known to be useful in solid form wherein Polyvinylpyrrolidone is carrier. See, particularly, col. 5, lines 33-63 in Sasatani et al. and the claims in Takada.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to formulate a pharmaceutical dosage form of the compounds disclosed by Andries et al. into solid dispersion or solution in particulate form, wherein vinypyrrolidone polymer or copolymer is the carrier, and with additional other pharmaceutical excipients, such as polyoxyethylene hydrogenated castor oil, citric acid.

A person of ordinary skill in the art would have been motivated to formulate a pharmaceutical dosage form of the compounds disclosed by Andries et al. into solid dispersion or solution in particulate form, wherein vinypyrrolidone polymer or copolymer is the carrier, and with additional other pharmaceutical excipients, such as polyoxyethylene hydrogenated castor oil, citric acid, because polymeric carrier, such as vinylpyrrolidone polymer or copolymer, are known to produce solid dispersion or solution with a drug which provide controlled release and enhanced bioavailability. Further, the employment of various pharmaceutical excipients, such as polyoxyethylene hydrogenated castor oil (surfactants), and citric acid (acids), accordingly is within the skill of artisan. The further employment of other polymers, such as hydroxypropylmethylcellulose, would have been obvious since the modified cellulose is known to be similarly useful as a solid carrier. Attention is directed to Baert, which teaches the employment of combination of PVP and hydroxypropyl methylcellulose as carrier for controlled release antiviral dosage form. See, particularly, the example (pages 6-7) and the claims.

Furthermore, the optimization of a result effective parameter, e.g., drug releasing profile, or the effective amounts of the drug and the other ingredients therein, is considered within the skill of the artisan. See, In re Boesch and Slaney (CCPA) 204 USPQ 215.

Art Unit: 1617

The employment of a dosage form known to be useful for a particular purpose, in a pharmaceutical package useful for the same purpose is considered within the skill of the artisan. Further, the optimization of a dosage regimen for the administration of a dosage form is considered within the skill of the artisan, absent evidence to the contrary.

***Response to the Arguments***

Applicants' amendments and remarks submitted December 13, 2005 have been fully considered, but are not persuasive.

Applicants allege an unexpected and unobvious benefit residing in the claimed invention, citing tables 1 and 2 for the allegation. There is no clear and convincing evidence in tables 1-2 for supporting alleged unexpected benefit. The data revealed in tables 1-2 is unclear, if not confusing. It is noted that examples 5 and 6 meet the limitation of claimed invention (see table 1). Table 2 labels these two examples as sustained release, but shows no such effect. The table shows these two examples have a sudden, almost complete release at 8 minute. Ironically, these labeled as instant release may sustain up to 120 minutes

Regarding the establishment of unexpected results, a few notable principles are well settled. It is applicant's burden to explain any proffered data and establish how any results therein should be taken to be ***unexpected and significant***. See MPEP 716.02 (b). The claims must be ***commensurate in the scope*** with any evidence of unexpected results. See MPEP 716.02 (d). Further, A DECLARATION UNDER 37 CFR 1.132 must compare the claimed subject matter with the closest prior art in order to be effective to rebut a prima facie case of obviousness. See, MPEP 716.02 (e).

Art Unit: 1617

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

**SHENGJUN WANG**  
**PRIMARY EXAMINER**  
Shengjun Wang  
Primary Examiner  
Art Unit 1617